3β-ol-20,21-dione dimethylacetal **6**,[12] mp 110—111°. By the same reaction sequence pregn-5-en-3β-ol-20-one acetate was converted to pregn-5-en-3β-ol-20,21-dione dimethylacetal in an overall yield of 71%.[13]

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12) During the initial stage of the present investigation, an 2-etianoyl-1,3-dithiolane was prepared in good yield by the reaction of ethane-1,2-dithiol ditosylate with 21-oxalylderivative of pregn-5-en-3β-ol-20-one with expectation that the dithioacetal group be hydrolyzed. But all attempts to hydrolysis by existing methods resulted in failure, occurring oxidation at C_2 of 2-acyl-1,3-dithiolane to give α-keto-ester or α-ketothiolester. Reported at 93th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, 1973.

13) Previously this conversion has been achieved usually by three step sequence ——21-acetoxylation with lead tetraacetate,[14] hydrolysis, and cupric acetate oxidation.[1,15] However, this method has intrinsic limitation for general application in that acetoxylation of methylketone bearing reactive double bond (*e.g.* **4**) dose not afford acceptable yield. Our method has its significance in that there exists no such limitation.

14) J.D. Cocker, H.B. Henbest, G.H. Phillips, G.P. Slater, and D.A. Thomas, *J. Chem. Soc.*, **1965**, 6; G.R. Pettit, C.L. Herald, and J.P. Yardley, *J. Org. Chem.*, **35**, 1389 (1970).

15) M.L. Lewbart and V.R. Mattox, *J. Org. Chem.*, **28**, 2001 (1963).

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Chemical Conversion of Adenosine to Guanosine (Nucleosides and Nucleotides. XI)[1]

A versatile chemical conversion of adenosine to guanosine is described. Treatment of adenosine-1-oxide with cyanogen bromide afforded hydrobromide salt of 2-imino-6-β-D-ribofuranosyl-(1,2,4-oxadiazolo[2,3-*f*]purine), which existed as N^6-cyanoadenosine-1-oxide on neutralization. Methylation of the latter followed by treatment with alkali afforded N^6-methoxy-2-aminoadenosine. The solvolysis of the product with liquid hydrogen sulfide gave 6-thioguanosine in high yield. Thioguanosine can be oxidatively hydrolyzed to guanosine by the known procedure. Catalytic hydrogenation of the oxadiazolopurine riboside in the presence of acetic acid gave 6-ureidopurine riboside.

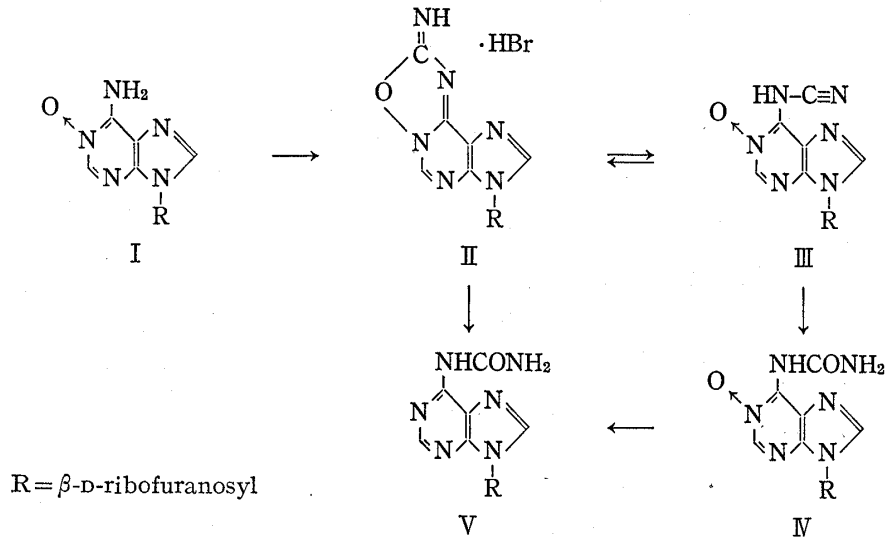
One of the most interesting chemical reactions in nucleic acid chemistry is a conversion of a certain nucleobase to another in nucleoside, nucleotide and polynucleotide levels. Such conversions have sofar been limited in the hydrolytic deamination of adenine- or cytosine- to hypoxanthine- or uracil-moiety.

We present here a versatile chemical conversion of adenosine to guanosine, through 6-thioguanosine, in relatively mild reaction conditions.

To a suspension of adenosine-1-oxide (I, 5 g)[2] in 400 ml of MeOH cyanogen bromide (2 g) was added and the mixture was stirred for one hour. The product, obtained in almost quantitative yield, was found to be 2-imino-6-β-D-ribofuranosyl(1,2,4-oxadiazolo [2,3-*f*] purine) hydrobromide(II, 6.3 g, 92%; *Anal.* Calcd. for $C_{11}H_{13}O_5N_6Br \cdot 1/3H_2O$: C, 33.43;

1) Part X: T. Ueda, K. Miura, M. Imazawa and K. Odajima, *Chem. Pharm. Bull.* (Tokyo), **22**, 2377 (1974).

2) M.A. Stevens, D.I. Magrath, H.W. Smith, and G.B. Brown, *J. Am. Chem. Soc.*, **80**, 2755 (1958).



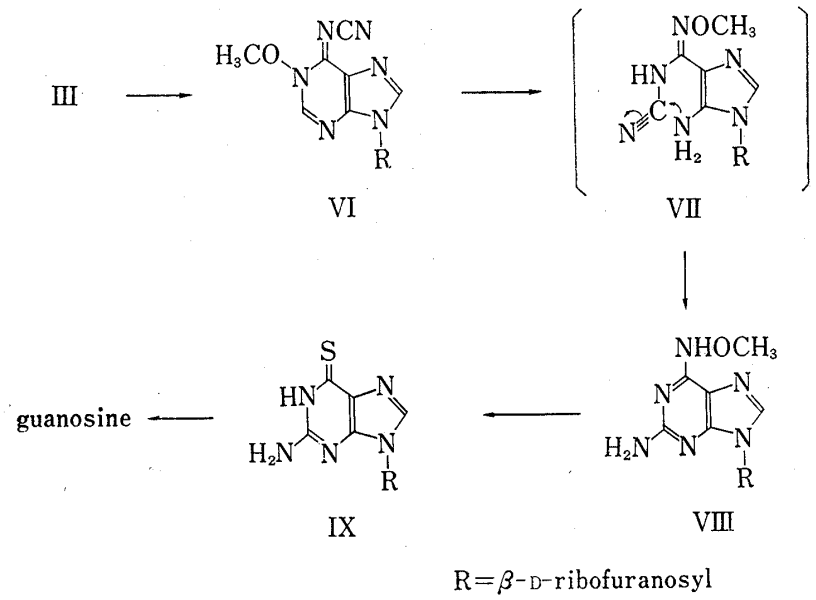
I II III IV V

Chart 1

H, 3.49; N, 21.27; Br, 20.22. Found: C, 33.54; H, 3.58; N, 21.46; Br, 20.27.). The ultraviolet (UV) spectra of II in water and 0.1 N HCl exhibited maxima at 225 and 285 nm which shifted to 247 and 293 nm in 0.1 N NaOH. The infrared (IR) spectra (KBr) showed no C≡N vibration but additional C=N at 1710 cm^{-1}. In nuclear magnetic resonance (NMR) spectra the signals of H-2 and H-8 were detected in lower magnetic field (10.10 and 9.07 ppm, respectively) than those of adenosines, suggesting a purinium structure of II.[3] Neutralization of II with methanolic ammonia resulted in a formation of N^6-cyanoadenosine-1-oxide (III), rather than the neutral form of II, which was confirmed by the detection of a strong and sharp C≡N vibration at 2160 cm^{-1} in IR and proton signals of 8.38 and 8.53 of H-2 and H-8 in NMR. The UV spectra of III (maxima at 247 and 293 nm in water and 0.1 N NaOH) were essentially identical with those of II in alkaline medium. It is to be noted that II and III are in pH-dependent equilibrium. Treatment of III with acetic acid afforded a ureidopurine (IV) which was hydrogenated over Pd-C catalyst to give 9-β-D-ribofuranosyl-6-ureidopurine (V), mp 169—172°. *Anal.* Calcd. for $C_{11}H_{14}O_5N_6$: C, 42.58; H, 4.55; N, 27.09. Found: C, 42.50; H, 4.59; N, 27.23. The catalytic hydrogenation of II in the presence of acetic acid also gave V in 53% yield.

Compound III was treated with methyl iodide in dimethyl formamide (DMF) at room temperature for 1.5 hour to yield N^6-cyano-1-methoxyadenosine (VI), 74%, mp 107°; UV $\lambda_{max}^{H_2O}$, 287 nm; IR (KBr), 2180 cm^{-1} (N–C≡N); NMR (DMSO-d_6, ppm): 8.88 (H-2), 8.59 (H-8), 5.90 (H-1′, d, J=5.1 Hz), 4.11 (N–OCH_3). *Anal.* Calcd. for $C_{12}H_{14}O_5N_6 \cdot 2/3H_2O$: C, 43.12; H, 4.42; N, 25.14. Found: C, 43.17; H, 4.61; N, 24.98. It was expected that the treatment of VI with base should give the ring-opened intermediate (VII) which recyclizes between 5-amino and 4-cyanamide group to furnish N^6-methoxy-2-aminoadenosine (VIII), as was found to be the case. Compound VI (644 mg) in 50 ml of EtOH and 5 ml of triethylamine was heated under reflux for 40 hours. The solid obtained after evaporation of the solvent showed NMR spectra consistent with the structure VIII; (DMSO-d_6, ppm), 9.93 ($N\underline{H}OCH_3$), 7.79 (H-8), 6.54 (NH_2), 3.75 ($NHOC\underline{H}_3$). The UV spectra ($\lambda_{max}^{H_2O}$, 281 nm, λ_{max}^{NHCl} 256, 293 nm) are also indicative of a 2,6-diaminopurine structure. A similar conversion of VI to VIII was performed by the treatment with 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) in EtOH under reflux for 1.5 hours. Compound VIII, without further purification, was treated with H_2S-

3) During the course of this study a report appeared in which the formation of an oxadiazoloquinoline from 2-aminoquinoline-1-oxide and cyanogen bromide was described: M. Hamana and S. Kumadaki, *Chem. Pharm. Bull.* (Tokyo), **22**, 1506 (1974).



R=β-D-ribofuranosyl

Chart 2

pyridine-H_2O in a sealed tube for 46 hours at 70°.[1,4] After the work-up 6-thioguanosine (IX) was obtained in a pure crystalline form (290 mg, 49% from VI) which was identical with the authentic sample[5] in every respect. Compound IX can be converted to guanosine in high yield by the known procedure.[6] In several runs of the above sequence of conversion the overall yield from adenosine to guanosine could be raised up to 31%. The present method can be applied to 2′-deoxyadenosine, arabinofuranosyladenine, tubercidin as well as the phosphoric esters of adenine nucleosides, and experiments on this account are currently being undertaken.

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